

CLAIMS

1. A method for predicting the level of ABCC2 activity in a patient comprising:
 - a) determining the sequence at position 3972 in one or both alleles of the *ABCC2* gene of the patient, wherein a C at position 3972 on one or both alleles is indicative of a normal level of ABCC2 activity.
2. The method of claim 1, wherein the sequence at position 3972 is determined for both alleles of the *ABCC2* gene.
3. The method of claim 2, wherein a T at position 3972 on both alleles of the *ABCC2* gene is indicative of a lower than normal level of ABCC2 activity.
4. The method of claim 1, further comprising obtaining a sample from the patient and using the sample to determine the sequence at position 3972.
5. The method of claim 4, wherein determining the sequence at position 3972 is performed by a hybridization assay, an allele specific amplification assay, or a sequencing or microsequencing assay.
6. The method of claim 4, wherein the sample comprises buccal cells, mononuclear cells, or cancer cells.
7. The method of claim 1, wherein the sequence at position 3972 is determined by evaluating the sequence of at least one position in linkage disequilibrium with the sequence at position 3972.
8. The method of claim 7, wherein the position in linkage disequilibrium with the sequence at position 3972 is selected from the group consisting of positions -1549, -1019, -24, and +27.

9. The method of claim 1, further comprising administering an ABCC2 substrate to the patient.
10. The method of claim 1, further comprising analyzing a clearance rate for an ABCC2 substrate.
11. The method of claim 10, wherein the substrate is selected from the group consisting of irinotecan, APC, and SN-38G.
12. The method of claim 1, wherein the patient is a cancer patient and wherein a C at position 3972 on one or both alleles is indicative of a lower probability of an antitumor response to an anticancer agent that is an ABCC2 substrate than the probability if the patient has a T on both alleles at position 3972.
13. The method claim 12, wherein the ABCC2 substrate is irinotecan.
14. The method of claim 12, further comprising administering the anticancer agent to the patient.
15. The method of claim 13, further comprising administering to the patient a second anticancer agent that is not an ABCC2 substrate.
16. The method of claim 12, further comprising prescribing a dosage of the anticancer agent based on determining the sequence at position 3972 in one or both alleles of the *ABCC2* gene.
17. A method for determining dosage of an ABCC2 substrate for a patient comprising:
 - a) determining the sequence at position 3972 in one or both alleles of the *ABCC2* gene of the patient, wherein a C at position 3972 on one or both alleles indicates a

higher dosage of the substrate than is indicated for a patient with a T at position 3972 in both alleles of the *ABCC2* gene.

18. The method of claim 17, further comprising obtaining a sample from the patient and using the sample to determine the sequence at position 3972.
19. The method of claim 18, wherein determining the sequence at position 3972 is performed by a hybridization assay, an allele specific amplification assay, or a sequencing or microsequencing assay.
20. The method of claim 18, wherein the sample comprises buccal cells, mononuclear cells, or cancer cells.
21. The method of claim 17, wherein the sequence at position 3972 is determined by evaluating the sequence of a position in linkage disequilibrium with a sequence at position 3972.
22. The method of claim 17, further comprising prescribing a dosage of the substrate based on determining the sequence at position 3972 in one or both alleles of the *ABCC2* gene.
23. A method for predicting risk of irinotecan toxicity in a patient comprising determining:
 - a) the sequence at position 3972 in one or both alleles of the *ABCC2* gene, wherein a C at position 3972 on one or both alleles indicates a lower risk of toxicity than a T at position 3972 in both alleles of the *ABCC2* gene;
 - b) the number, if any, of haplotype 4 in the *ABCC2* gene (-1549 A, -1019 G, -24 C, 1249 G, 34 T in intron 27, and 3972 T) of the patient, wherein one allele of haplotype 4 is indicative of a greater risk of toxicity than for a patient having two alleles with haplotype 4 but a lesser risk of toxicity than for a patient having no alleles with haplotype 4; and/or,
 - c) the sequence in one or both alleles of the *SLC01B1* gene at position 388, wherein
 - i) a G in one allele is indicative of a similar or lower risk than an A in one allele,

or ii) a G in both alleles is indicative of a lower risk than a G in one allele and an A in the other allele, which is indicative of a lower risk than an A in both alleles.

24. The method of claim 23, wherein the method comprises determining at least two of a), b) or c).

25. The method of claim 23, further comprising determining:

- d) the sequence in one or both alleles of the *UGT1A1* gene at position -3156, wherein i) a G in one allele is indicative of a similar or lower risk than an A in one allele, or ii) a G in both alleles is indicative of a lower risk than a G in one allele and an A in the other allele, which is indicative of a lower risk than an A in both alleles; and/or,
- e) the number of TA repeats in the promoter of the *UGT1A1* gene, wherein i) six TA repeats in one allele is indicative of a similar or lower risk than seven TA repeats in one allele, or ii) six TA repeats in both alleles is indicative of a lower risk than six TA repeats in one allele and seven TA repeats in the other allele, which is indicative of a lower risk than seven TA repeats in both alleles.

26. The method of claim 23, further comprising assaying total bilirubin amounts in the patient.

27. The method of claim 23, further comprising obtaining a sample from the patient and using the sample to make any determinations.

28. The method of claim 27, wherein determining any of 1), 2) or 3) is performed by a hybridization assay, an allele specific amplification assay, or a sequencing or microsequencing assay.

29. The method of claim 27, wherein the sample comprises buccal cells, mononuclear cells, or cancer cells.

30. The method of claim 23, wherein a sequence is determined by evaluating the sequence of a position in linkage disequilibrium with it.
31. The method of claim 23, further comprising prescribing a dosage of irinotecan based on determinations of at least 1), 2), and/or 3).
32. A method for predicting a clearance rate for irinotecan in a patient comprising
- a) determining the sequence of the patient at either 1) position 3972 in one or both alleles of the *ABCC2* gene, wherein a C at position 3972 in one or both alleles is indicative of a normal clearance rate for irinotecan; 2) position 521 in one or both alleles of the *SLCO1B1* gene, wherein a C at position 521 in one or both alleles is indicative of a lower clearance rate than a T in both alleles; or 3) both positions 1) and 2).
33. The method of claim 32, wherein the sequence at position 3972 is determined for one or both alleles of the *ABCC2* gene.
34. The method of claim 33, wherein a T at position 3972 on both alleles of the *ABCC2* gene is indicative of a lower than normal clearance rate for irinotecan.
35. The method of claim 32, further comprising obtaining a sample from the patient and using the sample to determine the sequence at position 3972.
36. The method of claim 35, wherein determining the sequence at position 3972 is performed by a hybridization assay, an allele specific amplification assay, or a sequencing or microsequencing assay.
37. The method of claim 35, wherein the sample comprises buccal cells, mononuclear cells, or cancer cells.

38. The method of claim 32, wherein the sequence at position 3972 is determined by evaluating the sequence of a position in linkage disequilibrium with a sequence at position 3972.
39. The method of claim 32, further comprising administering irinotecan to the patient.
40. The method of claim 38, further comprising prescribing a dosage of irinotecan based on determining the sequence at position 3972 in one or both alleles of the *ABCC2* gene.
41. A kit comprising, in suitable container means, at least one nucleic acid for determining the sequence at
- a) position 3972, 1549, -1019, -24, 1249, 34 in intron 27, and/or 3972 in an *ABCC2* gene; and/or
 - b) position 388 in a *SLC01B1* gene.
42. The kit of claim 41, further comprising at least one nucleic acid for determining:
- c) the sequence at position -3156 in a *UGT1A1* gene; and/or
 - d) the number of TA repeats in the *UGT1A1* gene promoter;.
43. The kit of claim 41, wherein the nucleic acid is a primer for amplifying the sequence(s).
44. The kit of claim 41, wherein the nucleic acid is a specific hybridization probe for detecting the sequence(s).
45. The kit of claim 44, wherein the specific hybridization probe is comprised in an oligonucleotide array or microarray.

46. The kit of claim 41, comprising at least one nucleic acid for determining the sequence of position 3972, 1549, -1019, -24, 1249, 34 in intron 27, and 3972 in an *ABCC2* gene (haplotype 4).